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10/642,926
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L1 STRUCTURE UPLOADED

=> s l1 full

L3 28 SEA SSS FUL L1

=> file ca

=> s 13

L4 3 L3

=> d ibib abs hitstr 1-3

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 140:16568 CA CA representation of aryl aniline .beta.-2 adrenergic receptor agonists

INVENTOR(S): Moran, Edmund J.; Jacobsen, John R.; Leadbetter, Michael R.; Nodwell, Matthew B.; Trapp, Sean G.; Aggen, James; Church, Timothy J.

BOURCE: USA: OLS Pat. Appl. Publ., 68 pp., Cont.-in-part of U.S. Ser. No. 292, 283.

CODEN: USXXCO

DOCUMENT TYPE: Patert

DOCUMENT TYPE:

Patent English 3 LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.	KIND	DATE		APPLICATION N	ο.	DATE
US 2003229058	A1	20031211		US 2003-43176	2	20030508
US 6670376	В1	20031230		US 2002-29283	5	20021112
US 2004059116	A1	20040325		US 2003-64292	6	20030818
US 2004063755	A1	20040401		US 2003-64319	6	20030818
PRIORITY APPLN. INFO.:			US	2001-338194P	P	20011113
			US	2001-343771P	P	20011228
			US	2002-292835	A2	20021112
			US	2002-292211	Al	20021112
OTHER SOURCE(S):	MA	RPAT 140:165	8			

Answer 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)
(prepn. of aryl aniline .beta.-2 adrenergic receptor agonists for
treatment of pulmonary disorders)
53064-66-3 CA
2(1H)-Quinolinone, 5-f(1R)-2-f(2-f4-f(6-ethoxy[1,1'-biphenyl]-3-y))amino]phenyl]ethyl]amino]-1-hydroxyethyl)-8-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

530084-87-8 CA

33004-6/-6 CA 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[(2-[4-[(6-methoxy[1,1'-bipheny]-3-yl)amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

530117-33-0 CA 2(1H)-Quinolinone, 8-hydroxy-5-[1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

Title compds. I [R1-5 = H, alk(en/yn)yl, cycloalkyl, heterocyclyl, etc.; R6 = H, alkyl, alkoxy; R7 = H, alkyl; R8 = H, alkyl; R9 = alk(en/yn)yl, (heterolaryl, etc.; R10 = H, alkyl; R1-13 = H, (cyclo)alkyl, alkenyl, alkenyl, alkynyl, (heterolaryl, etc.; p = 0-4] are prepd. For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl-.alpha.-bromocaetophenone (prepn. given) is reacted with 4-bromophenethylamine (CHZC12, EL3N) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4). The resulting protected amino alc. is then coupled with N-(4-heptyl-6-methyl-2-pyrimidinyl)sulfanllamide (PhMe, dppf, Pd2dba3, 80.degree., 5 h) and then deprotected with NGAC (80.degree., 5 h) to give II. All of the compds. tested demonstrated greater binding at the a.2

adrenergic receptor than at the .beta.l adrenergic receptor, i.e., Ki(.beta.l) > Ki(.beta.2); many with a selectivity greater than 20. I

are

useful for the treatment of pulmonary diseases.

530084-66-39-530084-87-89-530117-33-0P

530118-12-99-530118-13-99-530118-17-3P

530118-12-99-530118-13-99-530118-17-3P

530118-12-92-530118-21-99-530118-21-9P

530118-24-27-530118-22-0-87-530118-21-9P

631915-04-39-631915-05-4P-631915-06-5P

631915-04-79-631915-08-7P-631915-09-8P

631915-10-1P

RL: PAC (Fharmacological activity); SFN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREF (Preparation); USES

(Uses) IT

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

530117-43-2 CA 2[1H]-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued

●x HCl

RN 530118-10-6 CA
CN [1,1'-Biphenyl]-3-carbonitrile,
5'-[[4-[2-[(2R)-2-(1,2-dihydro-8-hydroxy2-oxo-5-quinolinyl)-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy(901) (CA YNDEX NAME)

Absolute stereochemistry.

RN 530118-11-7 CA CN [1,1'-Siphenyl]-3-carbonitrile, 5'-[[4-[2-[(2R)-2-(1,2-dihydro-8-hydroxy-2-oxo-5-quinolinyl]-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy-, trifluoroacetate (sait) (9CI) (CA INDEX NAME)

CM 1

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued

RN 530118-13-9 CA
CN 2(1H)-Quinolinone, 5-[(1R)-2-[(2-[4-[(4'-(aminomethyl)-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy-,
trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 530118-12-8 CMF C33 H34 N4 O4

Absolute stereochemistry.

CM 2

CRN 76-05-1 CMF C2 H F3 O2 L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued) CRN 530118-10-6 CMF C33 H30 N4 O4

Absolute stereochemistry.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 530118-12-8 CA
CN 2(1R)-Quinolinone, 5-[(1R)-2-[(2-{4-[[4'-{aminomethyl}]-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

RN 530118-17-3 CA
CN [1,1'-Biphenyl]-4-carboxaldehyde, 5'-[[4-[2-[[(2R)-2-(1,2-dihydro-8-hydroxy-2-oxo-5-quinolinyl)-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 530118-16-2 CMF C33 H31 N3 O5

Absolute stereochemistry.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

RN 530118-19-5 CA
CN 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[{2-[4-[[6-methoxy-4'(methylsulfonyl)[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]ethyl]-,
trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 530118-18-4

L4 MNSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN CMF C33 H33 N3 O6 S (Continued)

Absolute stereochemistry.

F-C-CO2H

530118-20-8 CA 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[(4'-hydroxy-6-methoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

со2н

RN 530118-24-2 CA
CN 2(1H)-Quinolinone,
5-[(1R)-2-[(2-[4-[(3'-chloro-6-methoxy[1,1'-biphenyl]-3y1)amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 530118-25-3 CA
CN 2(1H)-Quinolinone,
5-[(1R)-2-[(2-[4-{(3'-chloro-6-methoxy[1,1'-biphenyl]-3y1)aminolphenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy-, trifluoroacetate
(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 530118-24-2 CMF C32 H30 C1 N3 O4

Absolute stereochemistry.

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

530118-21-9 CA
2[IH]-Quinolinone, 8-hydroxy-5-[[IR]-1-hydroxy-2-[[2-[4-[(4'-hydroxy-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]ethyl]-,
trifluoroacetate (salt) [9CI] (CA INDEX NAME)

CM 1

CRN 530118-20-8 CMF C32 H31 N3 O5

Absolute stereochemistry.

CRN 76-05-1 CMF C2 H F3 O2

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

CM 2

CRN 76-05-1 CMF C2 H F3 02

RN 631914-89-1 CA
CN 2(1H)-Quinolinone,
8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[[6-methoxy-4'-[4morpholinylmethyl)[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]ethyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

RN 631915-04-3 CA CN [1,1'-Biphenyl]-3-carboxamide, 5'-[{4-[2-[((2R)-2-(1,2-dihydro-8-hydroxy-2oxo-5-quinolinyl)-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 631915-05-4 CA
CN 2(1H)-Quinolinone, 5-[(1R)-2-[[2-[4-[[3'-(aminomethyl)-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

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RN 631915-07-6 CA
CN 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[(2-[4-[[6-methoxy-3'[[[phenylmethyl]amino]methyl][1,1'-biphenyl]-3yl]amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

RN 631915-08-7 CA
CN 2(1H)-Quinolinone, 5-[(1R)-2-[[2-[4-[[3'-[(dimethylamino)methyl]-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

•x HCl

RN 631915-06-5 CA
CN 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[[6-methoxy-3'[[1]-methylethyl]amino]methyl][1,1'-biphenyl]-3yl]amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

14 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B

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RN 631915-09-8 CA

NN 2(1H)-Quinolinone, 8-hydroxy-5-[(IR)-1-hydroxy-2-[[2-[4-[[6-methoxy-3'-([(3-pyridinylmethyl)amino]methyl][1,1'-biphenyl]-3yl]amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

631915-10-1 CA
2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[[6-methoxy-3'-[[[(4-methoxyphenyi)methyl]amino]methyl][1,1'-biphenyl]-3yl]amino]phenyl]ethyl]amino]ethyl]- (SCI) (CA INDEX NAME)

L4 ANSWER 2 OF 3 CA
ACCESSION NUMBER:
138:401502 CA
Freparation of aryl aniline .beta.-2 adrenergic
receptor agonists
INVENTOR(S):
Moran, Edmund J.; Jacobsen, John R.; Leadbetter,
Michael R.; Nodwell, Matthew B.; Trapp, Sean G.;
Aggen, James; Church, Timothy J.
FATENT ASSIGNEE(S):
SOURCE:
PATENT ASSIGNEE(S):
FOR THE APPLICATION OF THE COORS.
FIXED COORS.
FIXED STATEMENT TYPE:
FAMILY ACC. NUM. COUNT:
FAMILY ACC.

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2003042164 A1 20030522 W0 2002-US36237 20021112

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CC, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, CE, GH, GM, HR, HU, ID, II, IN, IS, PF, KE, KG, KP, KR, KZ, LC, LX, LK, LK, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TT, TT, LUA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MM, MZ, SD, SI, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FT, FR, GB, GR, TE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, CQ, GW, ML, MR, NE, SN, TD, TG

US 2004059116 A1 20040325 US 2001-338194P P 20011113

US 2001-343771P P 200111228 1 20040325 US 2003-642926 20308018 US 2001-338194P P 20011113 US 2001-343771P P 20011228 US 2002-292211 A1 20021112 MARPAT 138:401502

OTHER SOURCE(S):

L4 ANSWER 1 OF 3 CA COPYRIGHT 2004 ACS on STN

(Continued)

PAGE 1-A

PAGE 2-A

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

Title compds. I [R1-5 = H, alk(en/yn)yl, cycloalkyl, heterocyclyl, etc.; R6 = H, alkyl, alkoxy; R7 = H, alkyl; R8 = H, alkyl; R9 = alk(en/yn)yl, (heterolaryl, etc.; R10 = H, alkyl; R1-13 = H, (cyclo)alkyl, alkenyl, alkynyl, (heterolaryl, etc.; p = 0-4) are prepd. For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl-alpha.-bromoactophenone (prepn. given) is reacted with 4-bromophenethylamine (CHZC12, EL3N) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NABH4). The resulting protected amino alc. is then coupled with N-(4-heptyl-6-methyl-2-pyrimdinyl)sulfarilamide (FNMe, dppf, PdZdba3, 80.degree., 5 h) and then deprotected with HOAc (80.degree., 5 h) to give II. All of the compds. tested demonstrated greater binding at the acceptance of the compds.

adrenergic receptor than at the .beta.l adrenergic receptor, i.e., Ki(.beta.l) > Ki(.beta.2); many with a selectivity greater than 20. I

Xi(.beta.1) > Ki(.beta.2); many with a selectivity greater than 20. I
useful for the treatment of pulmonary diseases.
530084-66-3P 530084-87-8P 530117-33-0P
530117-31-2P 530118-10-0F 530118-11-7P
530118-12-8P 530118-20-0F 530118-11-7P
530118-12-9P 530118-20-0F 530118-21-9P
530118-24-2P 530118-25-3P
RL: PAC (Pharmacological activity); SPN (synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preph. of aryl aniline .beta.-2 adrenergic receptor agonists for treatment of pulmonary disorders)
530084-66-3 cp.
530084-66-3 cp.
2(1H)-Quinolinone, 5-[(1R)-2-[(2-(4-[(6-ethoxy[1,1'-biphenyl]-3-y)] amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN Absolute stereochemistry. (Continued)

Absolute stereochemistry.

530117-33-0 CA 2(1H)-Quinolinone, 8-hydroxy-5-[1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-biphenyl]-3-y1) amino]phenyl]ethyl]amino]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

> CH-- OH Сн2

> > PAGE 2-A

PAGE 1-A

530117-43-2 CA 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-bipheny1]-3-y1)amino]pheny1]ethyl]amino]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

●x HC1

Absolute stereochemistry.

RN 530118-10-6 CA CN [1,1'-Biphenyl]-3-carbonitrile, 5'-[4-[2-[1(2R)-2-[1,2-dihydro-8-hydroxy-2-oxo-5-quinolinyl]-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy-(9CI) (CA INDEX NAME)

RN 530118-11-7 CA
CN [1,1'-Biphenyl]-3-carbonitrile,
5'-[[4-[2-[1(2R)-2-(1,2-dihydro-8-hydroxy2-oxo-5-quinolinyl]-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy-,
trifluoroacetate (salt) [9CI] (CA INDEX NAME)

CRN 530118-10-6 CMF C33 H30 N4 O4

Absolute stereochemistry.

Page 7

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN

CM 2

Absolute stereochemistry.

530118-13-9 CA 2{1H}-Quinolinone, 5-[(1R)-2-[[2-[4-[[4'-(aminomethyl)-6-methoxy[1,1'-

ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued) biphenyl]-3-yl]amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CRN 530118-12-8 CMF C33 H34 N4 O4

Absolute stereochemistry.

CM 2

CRN 76-05-1 CMF C2 H F3 O2

со2н

530118-17-3 CA
[1,1'-Biphenyl]-4-carboxaldehyde, 5'-[[4-[2-[[[2R]-2-[1,2-dihydro-8-hydroxy-2-oxo-5-quinolinyl]-2-hydroxyethyl]amino]ethyl]phenyl]amino]-2'-methoxy-, trifluoroacetate (salt) [9CI] (CA INDEX NAME)

CRN 530118-16-2 CMF C33 H31 N3 O5

Absolute stereochemistry.

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

CM 2

CRN 76-05-1 CMF C2 H F3 O2

со2н

530118-20-8 CA 2(1H)-Quinolinne, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[(4'-hydroxy-6-methoxy[1,1'-biphenyl]-3-y1)amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Page 8

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN

CM 2

CRN 76-05-1 CMF C2 H F3 O2

530118-19-5 CA 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[(2-[4-[[6-methoxy-4'-(methylsulfonyl)[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]ethyl]-, trifluoroscetate (salt) (9CI) (CA INDEX NAME)

CRN 530118-18-4 CMF C33 H33 N3 O6 S

Absolute stereochemistry.

ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued) 530118-21-9 CA 2(1H)-Quinolinone, 8-hydroxy-5-[(1R)-1-hydroxy-2-[[2-[4-[(4'-hydroxy-6-methoxy[1,1'-biphenyl]-3-yl]amino]phenyl]ethyl]amino]ethyl]-, trifluoroacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 530118-20-8 CMF C32 H31 N3 O5

Absolute stereochemistry.

CM 2

со2н

RN 530118-24-2 CA
CN 2(1H)-Quinolinone,
5-[(IR)-2-[(2-[4-[(3'-chloro-6-methoxy[1,1'-biphenyl]-3y1)amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry,

L4 ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

RN 530118-25-3 CA
CN 2(1H)-Quinolinone,
5-[(1R)-2-[(2-[4-[(3'-chloro-6-methoxy[1,1'-biphenyl]-3y1)amino]phenyl]ethyl]amino]-1-hydroxyethyl)-8-hydroxy-, trifluoroacetate
(salt) (9CI) (CA INDEX NAME)

CRN 530118-24-2 CMF C32 H30 C1 N3 O4

Absolute stereochemistry.

2

ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:

138:401501 CA
Preparation of aryl aniline .beta.-2 adrenergic TITLE:

Preparation or aryl anilhe .beta.-2 addenorgic receptor agonists
Moran, Edmund J.; Jacobsen, John R.; Aggen, James
Theravance, Inc., USA
PCT Int. Appl., 75 pp.
CODEN: PIXXD2
Patent INVENTOR (S): PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

English LANGUAGE:

OTHER SOURCE(S):

ANSWER 2 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN

Title compds. I [R1 = methoxy, ethoxy; R2 = H, Ph or R1 = H and R2 = phenyl; R3 = CHZOH, NHCHO; R4 = H or R3-4 = taken together are NHC(O)CH=CH] are prepd. For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl-.alpha.-bromoacetophenone (prepn. given) is reacted with 4-bromophenethylamine (CHZC12, EtN) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4). The resulting protected amino alc. is then coupled with 4-methoxy-3-phenylamiline (PhWe, dppf, PdZdba3, NaOBH-18, 80.degree., 5 h) and then deprotected with HOAC (80.degree., 5 h) to give II. All of the compds. tested demonstrated greater binding at the .beta.2 adrenergic receptor, i.e., Ki.(beta.1); many with a selectivity greater than 20. I are useful for the treatment of pulmonary diseases.

530084-34-5F 530084-35-6F 530084-43-6F 530084-37-8F 30084-63-F 530084-37-8F S30084-37-8F S30084-37

(Uses)
[prepn. of aryl aniline .beta.-2 adrenergic receptor agonists for treatment of pulmonary disorders)
50084-34-5 CA
2(1H)-Quinolinone, 8-hydroxy-5-[1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-biphenyl]-3-y1)amino]phenyl]ethyl]-, monohydrochloride (9CI)
(CA INDEX NAME)

L4 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

530084-35-6 CA
2(1H)-Quinolinone, 8-hydroxy-5-{(1R)-1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-bipheny]]-3-y]]amino]phenyl]ethyl]amino]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN

530084-53-8 CA 2(1H)-Quinolinone, 5-[2-[{2-[4-[(6-ethoxy[1,1'-bipheny1]-3-y1)amino]pheny1]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

530084-43-6 CA 2(1H)-Quinolinone, 8-hydroxy-5-(1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]ethyl]- (9Cl) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued)

530084-66-3 CA 2(1H)-Quinolinone, 5-{(1R)-2-[(2-[4-[(6-ethoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]-1-hydroxyethyl]-8-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

530084-87-8 CA 2(IH)-Quinolinone, 8-hydroxy-5-{(IR)-1-hydroxy-2-[[2-[4-[(6-methoxy[1,1'-biphenyl]-3-yl)amino]phenyl]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT: THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

L4 ANSWER 3 OF 3 CA COPYRIGHT 2004 ACS on STN (Continued) RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

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10/642,926
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=> file marpat

=> s 11 full

L5 4 SEA SSS FUL L1

=> s 15/com

L6 3 L5/COM

 \Rightarrow d ibib abs fqhit 1-3

L6 ANSWER 1 OF 3
ACCESSION NUMBER:
110:15568 MARPAT
Preparation of aryl aniline .beta.-2 adrenergic
receptor agonists
MORAN, Edmund J.; Jacobsen, John R.; Leadbetter,
Michael R.; Nodwell, Matthew B.; Trapp, Sean G.;
Aggen, James; Church, Timothy J.
USA
SOURCE:
USA. PAT. Appl. Publ., 68 pp., Cont.-in-part of U.S.
Ser. No. 292,635.
CODEN: USXXCO
Patent

US 2002-292835 US 2002-292211

Patent English DOCUMENT TYPE:

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE US 2003229058 US 6670376 US 2004059116 US 2004063755 US 2003-431762 20031211 Al Bl 20030508 US 2003-431/62 US 2002-292835 US 2003-642926 US 2003-643196 US 2001-338194P US 2001-343771P 20031230 20021112 20040325 20030818 20040401 20030818 PRIORITY APPLN, INFO.: 20011113 20011228

GI

ANSWER 1 OF 3 MARPAT COPYRIGHT 2004 ACS on STN (Continued)

= phenylene (SO (1-) G13) = Ph (SO (1-) G46) = 243

622-C(0)-G24

G44+G45= 197-6 194-1

or pharmaceutically acceptable salts and solvates additional substitution also claimed or stereoisomers

ANSWER 1 OF 3 MARPAT COPYRIGHT 2004 ACS on STN

AB Title compds. I [RI-5 = H, alk(en/yn)yl, cycloalkyl, heterocyclyl, etc.;
R6 = H, alkyl, alkoxy; R7 = H, alkyl; R8 = H, alkyl; R9 = alk(en/yn)yl,
(hetero)aryl, etc.; R10 = H, alkyl; R11-13 = H, (cycloalkyl, alkenyl,
alkynyl, (hetero)aryl, etc.; p = 0-4] are prepd. For instance, the di-Me
ketal of 4-hydroxy-3-hydroxymethyl-.alpha.-bromoacetophenone (prepn.
given) is reacted with 4-bromophenethylamine (CH2C12, Et3N) followed by
4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4).
The resulting protected amino alc. is then coupled with
N-(4-heptyl-6-methyl-2-pyrimidinyl) sulfanilamide (PhMe, dppf, Pd2dba3,
80.degree., 5 h) and then deprotected with HOAC (80.degree., 5 h) to give
II. All of the compds. tested demonstrated greater binding at the

adrenergic receptor than at the .beta.l adrenergic receptor, i.e., Ki(.beta.l) > Ki(.beta.2); many with a selectivity greater than 20. I

useful for the treatment of pulmonary diseases.

= 2

= 24-9 34-16

L6 ANSWER 2 OF 3 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:401502 MARPAT
TITLE: Preparation of aryl aniline .beta.-2 adrenergic receptor agonists
INVENTOR(S): Moran, Edmund J.; Jacobsen, John R.; Leadhetter, Michael R.; Nodwell, Matthew B.; Trapp, Sean G.; Aggen, James; Church, Timothy J.
PATENT ASSIGNEE(S): Theravance, Inc, USA
SOURCE: PIXTO CODEN: PIXTO CODEN: PIXTO PATENT INTERPMENTOR: English
FAMILY ACC. NUM. COUNT: BRITENT INTERPMENTOR: 10.

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

MO 2003042164 A1 20030522 WO 2002-US36237 20021112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GM, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, NM, MM, MX, NO, NZ, OM, PH, FL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TM, TR, TT, TZ, UR, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, MS, MS, MS, MS, TD, TG
US 2004059116 A1 20040325 US 2001-343771P 2001123 KIND DATE PATENT NO. APPLICATION NO. DATE US 2003-642926 20030818 US 2001-338194P 20011113 US 2001-343771P 20011228 US 2002-292211 20021112

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L6 ANSWER 2 OF 3 MARPAT COPYRIGHT 2004 ACS on STN

Title compds. I [R1-5 = H, alk(en/yn)yl, cycloalkyl, heterocyclyl, etc.; R6 = H, alkyl, alkoxy; R7 = H, alkyl; R8 = H, alkyl; R9 = alk(en/yn)yl, (heterolaryl, etc.; R10 = H, alkyl; R1-13 = H, (cyclo)alkyl, alkenyl, alkenyl, heterolaryl, etc.; p = 0-4] are prepd. For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl--alpha.-bromoacetophenone (prepn. given) is reacted with 4-bromophenethylamine (CHZC12, ELSN) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4). The resulting protected amino alc. is then coupled with N-(4-heptyl-6-methyl-2-pyrimidinyl)sulfanilamide (PhMe, dppf, Pd2db3, 80.degree., 5 h) and then deprotected with HOAC (80.degree., 5 h) to give II. All of the compds. tested demonstrated greater binding at the a.2

adrenergic receptor than at the .beta.1 adrenergic receptor, i.e., Ki(.beta.1) > Ki(.beta.2); many with a selectivity greater than 20. I

useful for the treatment of pulmonary diseases.

ANSWER 2 OF 3 MARPAT COPYRIGHT 2004 ACS on STN MPL:

claim 1
or pharmaceutically acceptable salts and solvates
additional substitution also claimed
or stereoisomers

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

ANSWER 2 OF 3 MARPAT COPYRIGHT 2004 ACS on STN (Continued)

= 24-9 34-16

= phenylene (SO (1-) G13) = O = Ph (SO (1-) G46) = 243 G12 G22 G31 G32

2932-C(O)-G24

G44+G45= 197-6 194-1

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L6 ANSWER 3 OF 3 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 138:401501 MARPAT
TITLE: Preparation of aryl aniline .beta.-2 adrenergic receptor agonists.
INVENTOR(S): Moran, Edmund J.; Jacobsen, John R.; Aggen, James PATEMT INCREMENT TYPE: CODEN: PTXXD2
DOCUMENT TYPE: LANGUAGE: PTAMEU ACC. NUM. COUNT: PTAMEU AC
     DOCUMENT TYPE:
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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PATENT NO.
                                                                                                                                               KIND DATE
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PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2003042160 A1 20030522 W0 2002-US36188 20021112

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BB, BP, BP, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, NA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, CM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SI, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TI, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, ES, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CZ, CM, GA, GN, GQ, GW, MI, MR, NE, SD, TD, TG

US 2003153597 A1 20030814 US 2002-292211 20021112

US 200405916 A1 20040325 US 2003-642926 20030818

PRIORITY APPLN. INFO:
                                                                                                                                                                                                                                                                                 US 2003-642926
US 2001-338194P
US 2002-292211
                                                                                                                                                                                                                                                                                                                                                                                              20011113
20021112
   GI
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L6 ANSWER 3 OF 3 MARPAT COPYRIGHT 2004 ACS on STN (Continued)

Title compds. I [R1 = methoxy, ethoxy; R2 = H, Ph or R1 = H and R2 = phenyl; R3 = CH2OH, NHCHO; R4 = H or R3-4 = taken together are NHC(0)CH=CH] are prepd. For instance, the di-Me ketal of 4-hydroxy-3-hydroxymethyl-.alpha.-bromoacetophenone (prepn. given) is reacted with 4-bromophenethylamine (CH2C12, EthN) followed by 4,4'-dimethoxychlorodiphenylamine and subsequently reduced (THF, NaBH4). The resulting protected amino alc. is then coupled with 4-methoxy-3-phenylamiline (PhMe, dppf, PdZdba3, NaSu-t, 80.degree., 5 h) and then deprotected with HOAc (80.degree., 5 h) to give II. All of the compds. tested demonstrated greater binding at the .beta.2 adrenergic receptor than at the .beta.1 adrenergic receptor, i.e., Ki(.beta.1) > Ki(.beta.2); many with a selectivity greater than 20. I are useful for the treatment of pulmonary diseases.

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L6 ANSWER 3 OF 3 MARPAT COPYRIGHT 2004 ACS on STN G1 = OMe G2 = Ph G3 + G4 = 31-8 34-7
                                                                                           (Continued)
쁈
              claim 1
or pharmaceutically acceptable salts or solvates
or stereoisomers
                                                THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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10/642,926
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FILE 'CA' ENTERED AT 15:44:10 ON 02 JUN 2004 L4 3 S L3

FILE 'MARPAT' ENTERED AT 15:44:44 ON 02 JUN 2004 L5 4 S L1 FULL

L6 3 S L5/COM

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L1

---Logging off of STN---

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Executing the logoff script...

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STN INTERNATIONAL LOGOFF AT 15:45:42 ON 02 JUN 2004